

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Currently amended) A substantially pure peptide comprising ~~an~~<sup>the</sup> amino acid sequence ~~selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2.~~
2. (Withdrawn) A substantially pure antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis.
3. (Withdrawn) The antibody of claim 2, wherein said antibody binds specifically to the about 30 kDa NH<sub>2</sub>-terminal polypeptide derivative of poly(ADP-ribose)polymerase produced in cells undergoing apoptosis.
4. (Withdrawn) The antibody of claim 2, wherein said antibody binds specifically to an epitope on a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2.
5. (Withdrawn) The antibody of claim 4, wherein said antibody binds specifically to an epitope comprising SEQ ID NO:1 on a peptide.
6. (Withdrawn) The antibody of claim 4, wherein said antibody binds specifically to an epitope comprising SEQ ID NO:2 on a peptide.
7. (Withdrawn) A method of detecting apoptosis in cells comprising the steps of:
  - (a) contacting a sample of cells with an antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis;
  - (b) determining by immunoassay the amount of the antibody which binds to the sample; and
  - (c) comparing the amount of antibody bound in step (b) with the amount of said antibody which binds to a sample known to be free of apoptosis.
8. (Canceled)
9. (Withdrawn) The method of claim 7 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which are attached to either said antibody or to a secondary antibody which recognizes said antibody.
10. (Withdrawn) The method of claim 9 wherein said immunoassay is selected from the group consisting of ELISA, cell-based ELISA, filter-binding ELISA, inhibition ELISA, Western blots, immunoprecipitation, slot or dot blot assays, immunostaining, RIA,

scintillation proximity assays, fluorescent immunoassays using antibody conjugates or antigen conjugates of fluorescent substances such as fluorescein or rhodamine, Ouchterlony double diffusion analysis, and immunoassays employing an avidin-biotin or a streptavidin-biotin detection system.

11. (Withdrawn) A method of detecting apoptosis in cells or tissue *in situ* comprising the steps of:

(a) contacting a fixed preparation of said cells or tissue with an antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis;

(b) determining by immunohistochemical analysis the amount of said antibody which binds to said preparation; and

(c) comparing said amount of antibody bound with the amount of antibody bound to cells or tissue not undergoing apoptosis.

12. (Canceled)

13. (Withdrawn) The method of claim 11 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which are attached to either said antibody or to a secondary antibody which recognizes said antibody.

14. (Withdrawn) The method of claim 11 wherein said cells or tissue include blood cells, biopsied cells, or tissue samples.

15. (Withdrawn) A method of diagnosing a disease, disorder, or condition associated with cell apoptosis comprising the steps of:

(a) contacting a sample of cells or tissue from a patient with an antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis;

(b) determining by immunoassay the amount of the antibody which binds to the sample; and

(c) comparing the amount of antibody bound in step (b) with the amount of said antibody which binds to a sample known to be free of apoptosis.

16. (Withdrawn) The method of claim 15 wherein said antibody binds specifically to an epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 on a peptide.

17. (Withdrawn) The method of claim 15 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which are attached to either said antibody or to a secondary antibody which recognizes said antibody.

18. (Withdrawn) The method of claim 15 wherein said immunoassay is selected from the group consisting of ELISA, cell-based ELISA, filter-binding ELISA, inhibition ELISA, Western blots, immunoprecipitation, slot or dot blot assays, immunostaining, RIA, scintillation proximity assays, fluorescent immunoassays using antibody conjugates or antigen conjugates of fluorescent substances such as fluorescein or rhodamine, Ouchterlony double diffusion analysis, and immunoassays employing an avidin-biotin or a streptavidin-biotin detection system.

19. (Withdrawn) The method of claim 15 wherein said disease, disorder, or condition is of a pathological or non-pathological origin.

20. (Withdrawn) A method of screening compounds to identify inhibitors of apoptosis comprising the steps of:

- (a) exposing a first and second sample of cells containing a protein which generates immunoreactive peptides during apoptosis to conditions known to trigger apoptosis in the cells;
- (b) contacting said first sample with a test compound;
- (c) contacting said first and second samples with an antibody which binds specifically to an epitope on said immunoreactive peptides;
- (d) determining by immunoassay the amount of the antibody which binds to said samples; and
- (e) comparing the amount of antibody bound in said samples;

wherein said test compound inhibits apoptosis if the amount of antibody bound to said first sample is less than the amount of antibody bound to said second sample.

21. (Withdrawn) The method of claim 20 wherein said immunoreactive peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2.

22. (Withdrawn) The method of claim 20 wherein said condition known to trigger apoptosis is contacting cells with a compound selected from the group consisting of etoposide, TNF-a, ceramide, and staurosporine.

23. (Withdrawn) The method of claim 20 wherein said condition known to trigger apoptosis is depriving cells of nerve growth factor or exposure to x-irradiation.

24. (Withdrawn) The method of claim 20 wherein said antibody binds specifically to an epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 on a peptide.

25. (Withdrawn) The method of claim 20 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which are attached to either said antibody or to a secondary antibody which recognizes said antibody.

26. (Withdrawn) A method of screening compounds to identify inhibitors of apoptosis comprising the steps of:

- (a) exposing a first and second mammal to conditions known to trigger apoptosis;
- (b) administering a test compound to said first mammal;
- (c) isolating a cell or tissue sample from said first and second mammals;
- (d) contacting said samples from said first and second mammals with an antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis;
- (e) determining by immunoassay the amount of the antibody which binds to said samples; and
- (f) comparing the amount of antibody bound in said samples;

wherein said test compound inhibits apoptosis if the amount of antibody bound to said sample of said first mammal is less than the amount of antibody bound to said sample of said second mammal.

27. (Withdrawn) The method of claim 26 wherein said antibody binds specifically to an epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 on a peptide.

28. (Withdrawn) The method of claim 26 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which

are attached to either said antibody or to a secondary antibody which recognizes said antibody.

29. (Withdrawn) The method of claim 26 wherein said mammal is a rodent.

30. (Withdrawn) A method of screening compounds to identify stimulators of apoptosis comprising the steps of:

(a) contacting a first sample of cells with a test compound;

(b) contacting said first sample and a second sample of cells with an antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis;

(c) determining by immunoassay the amount of the antibody which binds to said samples; and

(d) comparing the amount of antibody bound in said samples;

wherein said test compound stimulates apoptosis if the amount of antibody bound to said first sample is greater than the amount of antibody bound to said second sample.

31. (Withdrawn) The method of claim 30 wherein said antibody binds specifically to an epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2.

32. (Withdrawn) The method of claim 30 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which are attached to either said antibody or to a secondary antibody which recognizes said antibody.

33. (Withdrawn) A method of screening compounds to identify stimulators of apoptosis comprising the steps of:

(a) administering a test compound to a first mammal;

(b) isolating cell or tissue sample from said first mammal and from a second mammal not administered said test compound;

(c) contacting said samples from said first and second mammals with an antibody which binds specifically to an epitope on peptides produced in cells undergoing apoptosis;

(d) determining by immunoassay the amount of the antibody which binds to said samples; and

(e) comparing the amount of antibody bound in said samples;

wherein said test compound stimulates apoptosis if the amount of antibody bond to said sample of said first mammal is greater than the amount of antibody bound to said sample of said second mammal.

34. (Withdrawn) The method of claim 33 wherein said antibody binds specifically to an epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 on a peptide.

35. (Withdrawn) The method of claim 33 wherein the amount of antibody bound is determined using enzymic, chromogenic, radioactive, fluorescent or luminescent labels which are attached to either said antibody or to a secondary antibody which recognizes said antibody.

36. (Withdrawn) The method of claim 33 wherein said mammal is a rodent.

37. (Withdrawn) A kit for determining the amount of apoptosis-generated protein fragments in a biological sample comprising:

(a) a primary antibody which binds specifically to protein fragments generated during apoptosis; and

(b) a secondary antibody conjugated to a signal-producing label, wherein said secondary antibody binds specifically to said primary antibody.

38. (Withdrawn) The kit of claim 37 wherein said primary antibody binds specifically to an epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 on a peptide.

39. (Withdrawn) The kit of claim 37 wherein said signal-producing label linked to said secondary antibody is selected from the group consisting of enzymic, chromogenic, radioactive, fluorescent, and luminescent labels.

40. (Withdrawn) The kit of claim 37 wherein said signal-producing label linked to said secondary antibody is an enzyme and said kit further comprises a signal-producing tertiary reagent which reacts with said enzyme.

41. (Withdrawn) The kit of claim 40 wherein said enzyme is horseradish peroxidase or alkaline phosphatase.

42. (Withdrawn) The kit of claim 37 further comprising an uncoated support onto which a sample to be assayed, or said first antibody, can be immobilized.

43. (Withdrawn) A kit for determining the amount of apoptosis-generated protein fragments in a biological sample comprising:

(a) a primary antibody which binds specifically to protein fragments generated during apoptosis; and

(b) a secondary antibody conjugated to a signal-producing label, wherein said secondary antibody binds specifically to an apoptosis-generated protein fragment at an epitope different from that to which said first antibody binds.

44. (Withdrawn) The method of claim 7 or 11, wherein said protein fragments are produced from poly-ADP-ribose polymerase.

45. (Withdrawn) The method of claim 44, wherein said protease cleavage products are produced by a protease selected from the group consisting of ICE, CPP32/apopain/Yama, ICH-1, TX-ICH-2/ICE<sub>rel</sub>III, ICE<sub>rel</sub>III, MH-1/MH-3/ICE-LAP3, Mch2, FLICE/Mch5, and ICE-LAP6/Mch6.

46. (Withdrawn) The method of claim 7 or 11, wherein said protein fragments are produced from DNA replication complex C, DNA-dependent protein kinase, protein kinase of presenilin 1 or 2, or spectrin.

47. (New) A substantially pure peptide comprising a C-terminal amino acid sequence of SEQ ID NO:1.